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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/031,396 | 02/22/2002 | Junichi Miyazaki | 2002-0053 | 2281 |
| 513 | 7590 | 05/06/2004 | EXAMINER | |
| WENDEROTH, LIND & PONACK, L.L.P. | | | HILL, MYRON G | |
| 2033 K STREET N. W. | | | ART UNIT | |
| SUITE 800 | | | PAPER NUMBER | |
| WASHINGTON, DC 20006-1021 | | | 1648 | |

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/031,396

Applicant(s)

MIYAZAKI ET AL.

Examiner

Myron G. Hill

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 08 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1- 12 is/are pending in the application.
- 4a) Of the above claim(s) 5- 8 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1- 4 and 9- 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/18/02, 2/22/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 5- 8 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made of Group I **without** traverse in paper filed January 8, 2004.

Claims 1- 4, and 9- 11 are under consideration in this action.

Priority

The Office acknowledges the update of the first line of the specification to indicate that this application is a 371 of PCT/JP00/04815.

Information Disclosure Statement

Signed and initialed copies of IDSs filed January 18, 2002 and February 22, 2002 are enclosed.

Claim Objections

Claim 1 is objected to because of the following informalities:
"vector" is misspelled, the article "a" is missing from before "293 cell" and "line" is missing after "293 cell" in claim 4, and in claim 9, "where E1 region" should be "wherein the E1 region".

Appropriate correction is required.

Applicant is urged to carefully review the specification and claims for any additional errors.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1- 4 and 9- 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1- 4 are unclear because the method is incomplete. The method must end in a conclusion or a step that indicates that a rAd vector comprising a Ad genome and an expression cassette was made. It is not clear where the expression cassette comes from. Is it part of the cosmid or is it in the Ad genome to start with?

In claims 9- 11 it is not clear what structure is described that defines the vector. Where is the "site" recited in claim 9 located? Is the vector circular or linear in the claim?

In claims 1- 4 and 9- 11 it is not clear how the cosmid and the expression cassette relate to "where E1 or E1 and E2 regions are deleted".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1- 4 and 9- 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kojima *et al.* (Biochem. Biophys. Res. Com., 1998, Vol 246, pages 868- 872, from IDS), Chen *et al.* (Somatic Cell and Molecular Genetics, 1996, Vol. 22, pages 477- 488, from IDS), and Snaith *et al.* (Gene 1995, Vol 166, pages 173- 174, from IDS).

The claims are interpreted to mean the vector only requires a cosmid with recombinase ends and/or an expression cassette and that the adenovirus genome contains a deletion in E1 or E1 and E3.

Kojima *et al.* teach a method of constructing a recombinant cosmid/adenovirus vector comprising adenovirus and an expression cassette by the steps of constructing a cosmid/adenovirus vector by inserting and ligating a cosmid sequence with restriction sites at both ends to a adenovirus genome that has an E1 or E1 and E3 deletion (Figure 1). The adenovirus genome can also contain an expression cassette (Tet-luc, Figure 2). The cosmid sequences were removed from the vector (page 869, column 2, first full paragraph). Kojima *et al.* teaches that recombinase *Cre* can be used to regulate gene expression (page 872, column 1, lines 1 and 2).

Kojima *et al.* does not teach the use of recombinase sites to remove the cosmid sequences or transfection into cells with a recombinase expression vector.

Chen *et al.* teach that *Cre* is a recombinase that can cleaves loxP sites. This recombinase can be used with adenoviral vectors to induce deletions or

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rearrangements in adenoviral genomes defined by loxP sites (last line of abstract). Chen *et al.* teach that Cre can be used in manipulating the adenovirus genome (Figure 3b).

Snaith *et al.* teach that *Flp* is another recombinase similar to *Cre* and that the recognition sequence is FRT (page 173, column 1, first full paragraph).

One of ordinary skill in the art at the time of invention would have known that certain regions of the adenovirus genome can be deleted because they are not needed for growth in cell culture or the missing gene product can be supplied by cells expressing the missing protein. One of ordinary skill in the art at the time of invention would have known that cosmid vectors allow for the manipulation of DNA sequences in bacteria as opposed to mammalian cells that would be required for adenovirus itself. The method of Kojima *et al.* allows for manipulation of adenoviral genome without going through intermediate vector construction steps (page 868, column 2, second full paragraph). One would be motivated to modify the vector of Kojima *et al.* to use recombination sites because the cosmid/adenovirus vector could be transfected into a cell that expresses *Cre* and thus save the step in the method of Kojima *et al.* of purifying the cosmid/adenovirus vector and digesting it with restriction enzyme before transfecting cells to produce the recombinant virus. One of ordinary skill in the art at the time of invention would have known that the *Cre* of Chen *et al.* is an improvement over the prior art system of *Cre* expression of using a second vector to express the *Cre* (page 478, column 2, lines 3- 7). Kojima *et al.* teach that reduction of steps results in a more efficient system of making recombinant

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adenoviruses. One of ordinary skill in the art at the time of invention would have known that because of the size of the adenovirus genome, there are few restriction sites that can be used to cut the genome in one place. One would be motivated to use the *Cre* of Chen *et al.* because it has a longer recognition sequence that is not found in the adenoviral genome, and it would save a step in the cloning procedure and thus simplifying the complex manipulation.

Thus, it would have been *prima facie* obvious to make a cosmid/adenovirus vector by the method of Kojima *et al.* with the recombinase of Chen *et al.* with the expectation of success of making a recombinant cosmid/adenovirus vector with recombinase sequences one each end of the cosmid sequence that has deletions in the E1 or E1 and E3 and can have an expression cassette.

Conclusion

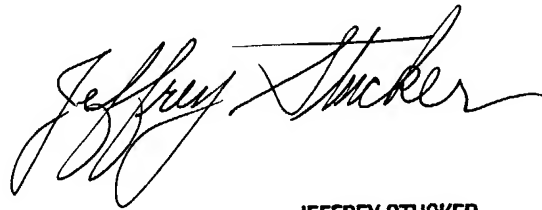
No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 571-272-0901. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

A handwritten signature in black ink, reading "Jeffrey Stucker". The signature is fluid and cursive, with the first name "Jeffrey" and last name "Stucker" clearly distinguishable.

JEFFREY STUCKER
PRIMARY EXAMINER

Myron G. Hill

Patent Examiner

April 27, 2004